

Claims

1. An isolated polynucleotide encoded by a phenotype associated (PA) gene; the polynucleotide is selected from the group comprising

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SEQ ID 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292 with allelic variation as indicated in the sequences section contained in a functional surrounding like full length cDNA for PA gene polypeptide and with or without the PA gene promoter sequence.

2. An expression vector containing one or more of the polynucleotides of claim 1.

30 3. A host cell containing the expression vector of claim 2.

4. A substantially purified PA gene polypeptide encoded by a polynucleotide of claim 1.
5. A method for producing a PA gene polypeptide, wherein the method comprises the following steps:
 - a) culturing the host cell of claim 3 under conditions suitable for the expression of the PA gene polypeptide; and
 - 10 b) recovering the PA gene polypeptide from the host cell culture.
6. A method for the detection of a polynucleotide of claim 1 or a PA gene polypeptide of claim 4 comprising the steps of:
 - 15 contacting a biological sample with a reagent which specifically interacts with the polynucleotide or the PA gene polypeptide.
 7. A method of screening for agents which regulate the activity of a PA gene comprising the steps of:
 - 20 contacting a test compound with a PA gene polypeptide encoded by any polynucleotide of claim 1; and detecting PA gene activity of the polypeptide, wherein a test compound which increases the PA gene polypeptide activity is identified as a potential therapeutic agent for increasing the activity of the PA gene polypeptide and wherein a test compound which decreases the PA activity of the polypeptide is identified as a potential therapeutic agent for decreasing the activity of the PA gene polypeptide.
 - 25 8. A reagent that modulates the activity of a PA polypeptide or a polynucleotide wherein said reagent is identified by the method of the claim 7.

9. A pharmaceutical composition, comprising:
the expression vector of claim 2 or the reagent of claim 8 and a pharmaceutically acceptable carrier.
- 5 10. Use of the reagent according to claim 8 for the preparation of a medicament.
- 10 11. A method for determining whether a human subject has, or is at risk of developing a cardiovascular disease, comprising determining the identity of nucleotide variations as indicated in the sequences section of SEQ ID 1-292 of the PA gene locus of the subject and where the SNP class of the SNP is "CVD" as can be seen from table 3; whereas a "risk" genotype has a risk ratio of greater than 1 as can be seen from table 6.
- 15 12. A method for determining a patient's individual response to statin therapy, including drug efficacy and adverse drug reactions, comprising determining the identity of nucleotide variations as indicated in the sequences section of SEQ ID 1-292 of the PA gene locus of the subject and where the SNP class of the SNP is "ADR", "EFF" or both as can be seen from table 3; whereas the probability for such response can be seen from table 6.
- 20 13. Use of the method according to claim 12 for the preparation of a medicament tailored to suit a patient's individual response to statin therapy.
- 25 14. A kit for assessing cardiovascular status or statin response, said kit comprising
 - a) sequence determination primers and
 - b) sequence determination reagents,

wherein said primers are selected from the group comprising primers that hybridize to polymorphic positions in human PA genes according to claim 1; and primers that hybridize immediately adjacent to polymorphic positions in human PA genes according to claim 1.

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15. A kit as defined in claims 12 detecting a combination of two or more, up to all, polymorphic sites selected from the groups of sequences as defined in claim 1.

- 10 16. A kit for assessing cardiovascular status or statin response, said kit comprising one or more antibodies specific for a polymorphic position defined in claim 1 within the human PA gene polypeptides and combinations of any of the foregoing.